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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/726,093	10/04/1996	MARTIN FUCHS	SYP-116(7783	8678

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EXAMINER
MARSCHEL, ARDIN H

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/726,093	Fuchs et al.
Examiner	**Art Unit**
Ardin Marschel	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Dec 31, 2002*

2a) [X] This action is **FINAL**. 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *135-145* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *135-145* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

Applicants' arguments, filed 12/31/02, have been fully considered but they are not persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

NEW MATTER

Claims 135-145 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 135 contains NEW MATTER because it cites, in part a, the contacting of a double-stranded nucleic acid sample with a PNA probe and a denaturing reagent which has not been found as filed. Applicants cite support for claim 135 in the specification on pages 9-11 and 13 and in the originally filed claims 1, 2, 6, 8, 10, and 11. These citations are responded to as follows. In the citation on page 9, line 14, through page 10, line 20, the contacting of the PNA probe with a double stranded nucleic acid sample occurs via PNA probe addition to the sample "which has been denatured". Thus, this citation lacks written basis for contacting of a double stranded nucleic acid sample with the PNA probe because the sample is no longer double

stranded at the time of addition or contact but rather "has been denatured" which is a prior conversion of nucleic acid from double to single stranded form. The remainder of the citation on page 9, line 14, through page 10, line 20, lacks any other written support for contacting a PNA probe with a double-stranded nucleic acid sample as now required in instant claim 135. It is noted that denaturing reagent practice is described on page 10, lines 15-17. The next support cited by applicants is on page 11, lines 9-24. In this citation on page 11 there is no specific contacting practice cited between a PNA probe and a double stranded nucleic acid sample. It is noted that raising the temperature to about 65 or greater is described on page 11, line 11, but without citing the presence of a denaturing reagent practice for denaturation. Thus, the page 11, lines 9-24, citation is reasonably interpreted as describing denaturing conditions via raising the temperature of a mixture rather than utilizing denaturing reagent(s) per se for this purpose. This citation therefore also lacks written support for the contacting step as now in claim 135. The citation to page 13, lines 3-16, describes salt conditions for preventing or disfavoring duplex formation but does not describe the contacting step a of instant claim 135 regarding contacting a double-stranded nucleic acid sample with a PNA probe with a denaturing reagent as now required in instant claim 135. It is also noted that higher salt

concentrations promote hybridization, rather than denaturation, and thus such salt practice has an effect which is opposite to a denaturing reagent, which would disfavor hybridization at higher concentrations. Lastly, applicants point to claims 1, 2, 6, 8, 10, and 11 as filed for written support. All of these claims depend directly or indirectly from claim 1 and therefore also contain the limitations of claim 1 as filed. Consideration of claim 1 as filed reveals that lines 1-3 therein disclose the sample as a "solution of single stranded nucleic acids and their complementary strands". This is clearly a sample description which lacks the double-stranded nucleic acid as now claimed in claim 135. In summary, claim 135 as now set forth contains NEW MATTER which has not been disclosed as filed. Claims 136-145 also contain this NEW MATTER due to their direct or indirect dependence from claim 135. This rejection is necessitated by amendment.

Claim 145 additionally contains NEW MATTER because it cites the PNA probe as being associated with a particle. The particle is cited in claim 145 without any further limitation as to the type of particle. Applicants point to page 5, line 8, for written support which describes "colored particles" as being a PNA probe label. Thus, there is written support for "colored particles" as labeling PNA probes, but not the broader generic "particle" as now set forth in claim 145. Consideration of the

other citation cited by applicants for support at page 12, lines 3-14, reveals that a resin is described therein but no written description as to what the resin is, nor that it is a particle as now present in claim 145. It is well known that a resin may be made in many forms such as a resin layer, particles, or resin solution to list a few examples. Additionally, the resin citation on page 12, lines 3-14, is utilized in connection with PNA probe synthesis and not during usage in contacting a PNA probe to a sample nucleic acid. Thus, this page 12 description cannot provide written basis for the particle limitation in instant claim 145 which depends from claim 135 wherein the PNA probe is present as step a as contacting the therein cited nucleic acid sample. This rejection is necessitated by amendment.

Claim 145 has been newly submitted to require the practice of PNA probe with an associated particle. This limitation contains NEW MATTER. This limitation is reasonably interpreted as indicating that electrophoretic mobility occurs regarding said PNA-particle probe as in claim 135, step b. Consideration of the instant disclosure as filed has failed to reveal a written description of this type of electrophoretically mobile PNA-particle. In the previous prosecution history of the instant application, applicants have pointed to the instant specification at pages 11, 13, 14, 27, 28, and in examples and figures for

support for this claim limitation. On said page 11, lines 9-24, hybridized PNA probe/DNA complex has a mobility different from unbound probe and single stranded nucleic acids and that the neutral PNA probe will not migrate in the gel. No particle content to the PNA probe is disclosed therein thus lacking support for claim 145 with an electrophoretically mobilizable PNA-particle type of probe. The description of mobility of the PNA probe/DNA complex implies that the PNA probe does not prevent electrophoretic mobility in the electrophoretic medium or gel. Since the electrophoretic gel mobility is clearly responsive to complex size, consideration of an added particle content would be required and is not described, however, on said page 11. Similarly, the other pages etc. have not been found to contain consideration of PNA-particle mobilizability in an electrophoretic gel or medium for size discrimination and thus also do not support this type of claim limitation as performed instantly. This therefore supports this rejection based on NEW MATTER. This rejection is necessitated by amendment.

VAGUENESS AND INDEFINITENESS

Claims 135-145 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite due to containing the

abbreviation, "PNA" as first present in claim 1, line 4. It is noted that the usage of this abbreviation in previous office actions caused a prior art rejection based on Weininger et al.(P/N 5,871,902) due to Weininger et al. also utilizing the abbreviation, "PNA" but therein confusingly indicating a molecule which is different from the apparent instant peptide nucleic acid type molecule. Clarification of the claim wording to remove this unclarity is requested. This rejection is necessitated by amendment which brought back the PNA abbreviation, which had previously been replaced by the full name thereof. Claims 136-145 also contain this NEW MATTER due to their direct or indirect dependence from claim 135.

PRIOR ART REJECTION

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 135-144 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rose [Analytical Chem. 65:3545(1993)], taken in view of Chen et al.(Ref. CN); taken in view of Cummins et al.(P/N 6,045,995) for various PNA label embodiments as well as Nielsen et al.(P/N 5,539,082) for other labels on PNA probes; taken further by Fuchs et al. (P/N 5,630,924) regarding electrophoresis in a channel in a substrate.

This rejection is necessitated by amendment which changed the invention from apparati and separation methods to detection method claims.

Rose discloses the separation of PNA/nucleic acid complexes from hybridized nucleic acid/nucleic acid duplexes by capillary electrophoresis. A PNA probe either displaces its complementary oligonucleotide from a DNA duplex as is shown in Figure 7 on page 3549 as being separated from the other components in the mixture, or, alternatively, the PNA probe hybridizes to the complementary single stranded target nucleic acid as shown via results and corresponding discussion in Figures 2 or 3 on pages 3546 and 3547, respectively. These alternative sample types are pointed to regarding this rejection as options of the instant claims, if the above NEW MATTER is removed or not, thus resulting in claim practice with either single or double stranded target nucleic

acid sample practice, respectively. This is also described on page 3549, second column, first full paragraph. The PNAs are detectably labeled via nucleobases that are detectable by 260 nm absorbance, however, PNA hybridization probes may be alternatively labeled as discussed below. The PNA that is depicted on page 3546 of the reference contains a charge-modifying moiety as given in instant claim 144 in that the upper terminus of the structure contains an amine moiety that results in a normally present "plus" charge that is modified compared to the terminus without this amine moiety which would be a carboxyl which is normally negatively charged. This charge modification is also discussed on page 3546 in the sentence that bridges the first and second columns. The reference's capillary contains a sieving medium as is also a limitation of instant claim 137.

Rose has been summarized above but lacks disclosure of the practice of gel in the capillary electrophoresis apparatus as containing polyacrylamide as given in instant claim 138. Rose, however, suggests and motivates generic capillary electrophoresis on page 3546, first column, lines 3-8, as being of the type also utilized for DNA-DNA duplex analysis as given in Chen et al. (Ref. CN).

Chen et al. (Ref. CN) discloses capillary electrophoresis therein as utilizing polyacrylamide filled gel capillaries as given in the abstract and on page 296, last paragraph, and in

Figure 1 on page 299. It is noted that Chen et al. also suggests and motivates the use of urea as a denaturant of double stranded nucleic acids on page 298 in the section entitled "Dissociation of the hybridized species by urea and heat" as an option as also given in the instant claims.

Cummins et al. also is a reference directed to capillary electrophoresis for the analysis of PNA/DNA hybridization. The probes of Cummins et al. are additionally described as being labeled with a variety of labels such as fluorescein etc. in column 3, lines 18-37, and in column 9, lines 3-55. The polyacrylamide gel capillary electrophoretic medium is described in column 3, lines 55-59. These probes may be preferably of the PNA type as described in column 8, lines 54-67. The PNA probe hybridization to target nucleic acid being favored over DNA/DNA or DNA/RNA hybridization for electrophoretic separation and detection of hybrids is described in Cummins et al. in column 13, lines 12-25.

Nielsen et al. expands on Cummins et al. as summarizing other PNA probe labels including enzymes and biotin in column 9, lines 12-30.

Fuchs et al. suggests and motivates the functional equivalence of electrophoretic separation of mixtures of molecules via various types of electrophoretic methods in tubes, capillaries, and channels in column 1, lines 12-27. This is

described more in detail starting in column 7, line 40. Fuchs et al. also describes advantages of the electrophoretic separation methods therein described in column 6, lines 45-67, as being ultrafast as well as permitting detectable enzyme labels usage. Fuchs et al. clearly describes a broad range of analyte/binding partner options in column 8, lines 10-67, which generically encompass prior art assay types which are reasonably deemed to include the hybridization assay types in such prior art as that of Rosen (above) and Chen et al.(above) in such a broad listing as in Fuchs et al. The channel in a substrate electrophoretic practice of instant claim 140 is described in Fuchs et al. at several citations and, in particular for example, at column 19, line 44, through column 22, line 38, as well as in column 14, line 64, through column 15, line 15, specifically describes electrophoretic separation of particular complexes with column 15, line 52, through column 18, line 67, giving generic electrophoretic descriptions for generic binding partner assay types.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the instant invention because Rose gives the basic methodology and suggests and motivates, by specific reference, the capillary gel electrophoresis methodology of Chen et al. (Ref. CN) as being the type of electrophoretic practice therein being investigated.

Chen et al. (Ref. CN) discloses both capillary electrophoresis as being performed with polyacrylamide in the capillary gel and optionally urea for denaturation. These references are expanded on by Cummins et al. and Nielsen et al. regarding functionally equivalent labels for PNA probes thus resulting in these embodiments of the instant invention. Fuchs et al. further motivates and suggests channel in a substrate practice broadly for any electrophoretic analyte/binding partner type assay, which is deemed to generically include the instant PNA based binding assay type thus resulting in the practice of the instant invention.

INFORMALITIES

The disclosure is objected to because of the following informalities:

Claim 135 contains improper periods within the claim. The periods after the subpart designations set forth as "a.", b.", and "c." are improper. It is suggested to amend claim 135 to designate the subparts as "a)" etc.

Appropriate correction is required.

No claim is allowed.

Applicants' amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)305-3014 or (703)308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

April 28, 2003

Ardin H. Marschel